

II. REMARKS

Claims 1-9 and 11-15 are pending in the subject application. By this response, claims 1, 2 and 11 to 15 are amended. The amendments to the claims are not intended to be a dedication to the public of the subject matter of the claims as previously presented or the equivalents thereof. Support for the claims as amended can be found throughout the specification as filed, for example, support for the term "reconstituted powders," such as reconstituted dairy-based powders, can be found on page 3 lines 14 to 17, page 6, lines 23 to 30 and page 10 line 1 to line 9. Page 6, lines 23 to 30 of the description describe the preparation of a number of different media, and specifically, this passage describes the preparation of 10% solutions of media such as reconstituted demineralized whey powder, reconstituted whey protein concentrate powder. The term "food-grade" is supported on the specification on page 12, line 1 to page 13, line 17. Page 10, line 1 to line 9 of the specification describes various media that include reconstituted yeast powders such as TY broth. Amended claim 13 is supported throughout the specification and in particular, on page 2, line 26 to page 3 line 2; page 4 lines 5 to 8; and pages 12 to 13.

When?
any
13-15

An issue of new matter is not raised by these amendments and entry thereof is respectfully requested. The amendments were not made earlier as it is Applicant's position that the claims as previously presented patentable subject matter. The claims have been amended to place the case in condition for allowance or in better form for appeal.

In view of the preceding amendments and the remarks that follow, reconsideration and withdrawal of the rejections set forth in the Final Office Action is respectfully requested.

35 U.S.C. § 112, Second Paragraph

Claims 1 to 9 and 11 to 15 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter of the invention. Without conceding the correctness of the Office's position, the claims have been amended as

suggested by the Office to remove the grounds for rejection. In view of the preceding amendments, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph is respectfully requested.

35 U.S.C. § 102(b)

Claims 11-13 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by McAuliffe et al., of record, published February 1999 (vol. 2). The Office noted that Applicants' arguments filed September 13, 2002 were considered, but failed to overcome the rejection. The Office remarked that

“At page 5 of the response, applicants state that the product of McAuliffe et al. is produced by bacteria grown in a “complex nutrient medium” which is not suitable as a food ingredient, and therefore is not a commercial food additive. This is not deemed persuasive, as a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). It is noted, however, that only claims 11-13 have been rejected. These claims do not recite a “food ingredient”, nor any other intended use. As stated in the rejection under 35 U.S.C. 112, second paragraph above, claim 13 fails to further define over the product of claim 11 or 12, as no further components are recited that would serve to distinguish the “food product comprising a spray-dried lacticin 3147” in claim 13, over the “spray-dried lacticin 3147” of claims 11-12.

Applicants state that “the product claimed is not lacticin 3147, [but rather] it is a concentrate capable as a formulation as a spray-dried powder.” This is not deemed persuasive, as claim 12 is specifically drawn to a “spray-dried lacticin 3147.” No other components are present. It is not claimed as a concentrate”, or as part of a “spray-dried powder *containing* lacticin 3147.” As previously stated on the record, lacticin 3147 in any form, spray-dried or otherwise, is still the same compound. The preparation of a known product in a specific physical form does not render novel said known product.”

Applicants respectfully traverse. The claims have been amended to more specifically point out that the composition is for use in foods. As noted in Applicants' prior response, McAuliffe et al. does not teach or suggest a method or system for the preparation of a food-grade concentrate comprising lacticin 3147. In view of the amendment of the claims, McAuliffe et al. clearly does not teach each and every element of the claims. Accordingly, removal of the rejection of amended claims 11-13 under 35 U.S.C. § 102(b) is respectfully requested.

Claims 11 to 15 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ryan et al. (WO 96/32482, previously cited). The Office considered Applicants' arguments set forth in the reply to the first substantive Action, but they were not considered persuasive. The Office stated that

“[A]t page 5 of the response, applicants state that Ryan discloses a freeze-dried powder, whereas the instant claims describe the production of a “concentrate made by a different process and therefore having different physical properties, e.g. it that [sic] may be formulated as a spray-dried powder.” This is not deemed persuasive for the reasons of record. Applicants have provided no support for the statement that the dried powder of Ryan et al. is physically different from the dried powder of the instant claims. As stated above, a structural difference must exist between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, and/or possesses the same physical properties, then it meets the claim. In a claim drawn to a product-by-process, the process must result in a manipulative difference in the product, as compared to the prior art. As previously stated on the record, lacticin 3147 in any form, spray-dried or otherwise, is still the same compound. The preparation of a known product in a specific physical form does not render novel said known product.”

Applicants respectfully traverse. As stated above, the claims have been amended herein to more specifically point out and distinctly claim that the composition is for use in foods. Ryan et al. does not teach or suggest the invention because the authors do not disclose how to make nor have they made a food-grade composition. Ryan et al. also discloses purified lacticin composition. Applicants' invention, in contrast, is not purified lacticin, it is a composition

enriched with lacticin, and therefore contains a mix of proteins and peptides. Moreover, the product claimed by the present application is not lacticin 3147, it is a spray-dried concentrate comprising lacticin 3147 which is quite distinct from the product disclosed in Ryan *et al.*

In other words, the *spray-dried* powder of the present invention was developed as a food ingredient and it is the result of a food-grade fermentation process. Again, the *spray-dried* powder of the present invention has not been purified at all and will contain many other food grade fermentation products. In contrast in Ryan *et al.* the *freeze-dried* lacticin described is the result of a purification protocol in which lacticin has been isolated from all other contaminating peptides and proteins. Moreover the purification is achieved using non-food grade chemicals (which include acetone) and as such the resulting lacticin 3147 would not be suitable for consumption. Thus, the reference fails to anticipate because it does not describe a method to prepare a spray-dried food-grade concentrate. The final composition also is different in that Ryan *et al.* discloses an isolated lacticin where as Applicant's composition has not been purified prior to processing.

In view of the preceding amendments and remarks, reconsideration and withdrawal of the rejection of claims 11 – 15 under 35 U.S.C. § 102(b) as anticipated by Ryan *et al.*

35 U.S.C. § 103(a)

The Office maintained the rejection of claims 1-9 and 11-15 under 35 U.S.C. § 103(a) as allegedly unpatentable over Ryan *et al.* (WO 96/32482), in view of DE 2616390 (English abstract provided).

The Office rejected Applicants' argument that "many bacteriocins are heat labile", and that there is even "a class of bacteriocins which are called heat-labile bacteriocins." The Office argued that Applicants' prior remarks do not speak to the specific lacticin compound as claimed, namely lacticin 3147. The Office also noted that not all claims are directed to a spray-drying

process step, or a spray-dried product, and that the features upon which applicant relies (i.e., spray-drying) are not recited in the rejected claim(s).

The Office also opined that Applicants "potential failure" scenarios are unsupported on the ground that the cited references demonstrate a reasonable expectation of success, both from the knowledge in the art concerning the lacticin 3147 compound itself, and the general state of the art of spray-drying other bacteriocin compounds. The Office took note that both lacticin 3147 and nisin (DE 2616390) are derived from strains of the *same species and subspecies* of bacteria, namely *Lactococcus lactis*, subsp. *lactis*, and that thus, the thermostability of one compound must be at least equal to that of the other, in order for the microorganism to survive at a particular temperature, and for the compounds to be active at such temperatures.

The Office remarked that regarding the concept of dehydration of the lacticin protein, it is noted that *Lactococcus lactis*, subsp. *lactis* microbes are shipped from the ATCC depository freeze-dried, and thus it would not be expected that a dehydration of the *medium* in which the lacticin protein is present, would yield additional difficulty.

The Office further remarked that one of ordinary skill in the art would indeed have known much about the thermostability of lacticin 3147, since it is alleged to be a well-characterized protein, known in the art for decades. To support this position, the Office made reference to page 439, col. 1, of McAuliffe et al., 1998 (submitted in the most recent IDS), which states that "lacticin 3147 is a bacteriocin produced by *Lactococcus lactis*, subsp. *lactis* DPC3 147 ... [and] is a heat-stable compound."

Applicants respectfully traverse and note that the claims have been amended to more specifically point out and distinctly claim the subject matter of the invention. Applicants maintain that the Office has failed to support a *prima facie* case of obviousness. Each of the Office's rebuttal arguments are individually responded to below.

Applicants note that it was stated that lacticin 3147 was heat stable by McAuliffe *et al.*, and that Ryan *et al.* report on page 16 (and figure 6) a temperature stability study in which the temperature range under investigation was from 60°C to 121°C. At 110°C, 50% of lacticin 3147 activity was lost at pH 7.

Applicants maintain that this is not an unusual finding. In fact many bacteriocins are heat labile, such as enterolysin and colicin; indeed as previously pointed out there is a class of bacteriocins that are actually called heat-labile bacteriocins. The teaching available prior to the development of the invention would indicate to the person skilled in the art that there was a strong possibility that spray-drying would result in a significant loss in lacticin 3147 activity. In sum, the teachings of the prior art as a whole lead away from my reasonable expectation of success as now shown by Applicants.

Moreover, the temperatures required to spray dry the fermentate of the present invention includes an inlet temperature of about 190°C and an outlet temperature of about 90°C. The temperature of 190°C is much higher than the temperatures studied in Ryan *et al.* so the skilled person could not have predicted on reading Ryan *et al.* that the lacticin 3147 could have remain active at high levels following exposure to a temperature of 190°C. It was not known, and could not have been predicted on reading Ryan *et al.* or DE 2616390, that lacticin would retain any activity following exposure to the high temperature conditions involved in spray-drying; and so it would not be obvious, to a person skilled in the art, to adapt the process of DE 2616390 to form spray-dried lacticin 3147.

In response to the Office's position that "*It is noted that both lacticin 3147 and nisin (DE 2616390,) are derived from strains of the same species and subspecies of bacteria, namely Lactococcus lactis, subsp. lactis. Therefore, the thermostability of one compound must be at least equal to that of the other...*" Applicants submit that this argument is not supported in biology. An analogous argument would be to state that two related although structurally different proteins such haemoglobin and myoglobin can be both derived from the same species and

therefore the thermostability of one compound must be at least equal to that of the other. This is of course not true. In fact if it were many purification techniques commonly used in the laboratory would not work. Applicants point out that lacticin and nisin differ considerably, particularly since lacticin is a two-component bacteriocin (mentioned in McAuliffe *et al.* page 440-441) whereas nisin is a single peptide. It is important to note that the lacticin 3147 must survive the spray drying process as a two-component peptide in order for activity to remain. This is a very different situation to a single nisin peptide surviving high temperature treatments.

Furthermore the Examiners argument that “...*in order for the microorganism to survive at a particular temperature, and for the compounds to be active at such temperatures*” does not take into account the natural environment of *Lactococcus lactis*, namely cattle udders and dairy products. At no time in its life cycle is *Lactococcus lactis* exposed to temperatures ranging up to about 190°C. There is no literature suggesting that *Lactococcus lactis* would survive at this temperature. Therefore it is surprising that a bacteriocin produced by this species is still active following exposure to such stringent denaturing conditions. Moreover, it is important to re-emphasise that lacticin 3147 is very distinct from nisin. In Ryan *et al.* there is a specific section outlining the fact that the lacticin 3147 producer is not a nisin producer, in particular see the discussion on pages 15-16.

On page 6 of the Final Office Action the Examiner maintains that “*Regarding the concept of dehydration of the lacticin protein, it is noted the Lactococcus lactis, subsp. lactis microbes are shipped from the ATCC depository freeze-dried, and thus it would not be expected that a dehydration of the medium in which the lacticin protein is present, would yield additional difficulty*”. Applicants note that it can also be argued that while the *Lactococcus lactis* bacteria itself can survive the freeze-drying process, it is unknown that any bacteriocin produced by *Lactococcus lactis* would survive in an active form. It can be argued that any bacteriocin detected following re-animation of freeze-dried *Lactococcus lactis* could be due to the bacteria

producing fresh bacteriocins. Simply put, it would not be obvious to a person skilled in the art that lacticin 3147 would survive the freeze-drying process.

On page 6 of the Final Office Action the Examiner states that *"It is important to note that applicants' arguments are conflicting, as the statements at page 7 appear to imply the direct dehydration of the lacticin alone, which is not claimed, yet applicants had also stated at page 5, 'the product claimed is not lacticin 3147', but rather a concentrated culture media containing the protein."* Applicants point out that the statements made on page 7 of the response filed in September of 2002 all refer to a spray-dried lacticin 3147 concentrate. The Office incorrectly concludes that Applicants were implying that a lacticin 3147 concentrate is equivalent to isolated or purified lacticin 3147 alone. Indeed, the statements made on page 7 are quite consistent with those made on page 5. Again, Applicants emphasize that product claimed is not purified lacticin 3147, but rather a concentrate comprising a food-grade spray-dried lacticin 3147.

In sum, the Office's stated reasons for rejection of the claims under 35 U.S.C. § 103 are based on impermissible hindsight analysis. There is no teaching or enablement in the references regarding how to achieve a food-grade concentrate containing lacticin 3147.

In view of the preceding amendments and remarks, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103, is respectfully requested.

III. CONCLUSION

Applicants respectfully request entry of the amendment and reconsideration of the claims. A notice of allowance is earnestly solicited. In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2518**, referencing

attorney docket no. 24005-7002. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

If a telephone interview would advance examination of the subject application, the Examiner is invited to telephone Antoinette Konski at 650-849-4950.

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Respectfully submitted,

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Version of the Proposed Amendments to the Claims

with Markings to Show Changes Made

In the Claims:

1. (Twice Amended) A process for the production of a spray-dried concentrate comprising lacticin 3147, for use as a food ingredient, comprising:
 - (a) inoculating a food-grade medium with a lacticin 3147-producing strain of bacteria;
 - (b) fermenting the inoculated medium;
 - (c) adjusting the pH of the fermentation to a pH ranging from 6.3 to 6.7;
 - (d) inactivating the bacteria within the fermentate; and
 - (e) evaporating the fermentate of step (d) thereby producing the lacticin 3147 concentrate for use as a food ingredient.

2. (Twice Amended) A process as claimed in claim 1, wherein the medium of step (a) is selected from the group consisting of milk, reconstituted dairy-based powders, reconstituted demineralized whey powder, reconstituted skimmed milk powder, reconstituted whey protein concentrate powder, pasteurized whole milk, Cheddar cheese whey, reconstituted yeast powders, and synthetic laboratory-type media.

11. (Twice Amended) A concentrate comprising a food-grade spray-dried lacticin 3147 produced by the process of any one of claims 1 to 9.

12. (Twice Amended) A spray-dried food-grade powder containing lacticin 3147 having the ability to inhibit organisms which are not resistant to lacticin 3147, and having an activity of greater than about 20,000 AU/ml.

13. (Twice Amended) A food product comprising a lacticin 3147 enriched spray-dried food-grade fermentate produced by the process of any one of claims 1 to 9 and a foodstuff.

14. (Twice Amended) The food product as claimed in claim 13, wherein said product is selected from the group consisting of an infant milk formulation, a sauce, a mayonnaise, a dessert including a custard, a tinned food, a yogurt, a soup and a bakery product.

15. (Twice Amended) A food product as claimed in claim 13 and 14, which has been subjected to hydrostatic pressure in the range from about 150 MPa to about 800 MPa.